Article

CLINICAL REHABILITATION

Clinical Rehabilitation
2017, Vol. 31(12) 1616–1624

DOI: 10.1177/0269215517709052
journals.sagepub.com/home/cre
SAGE

Six-month effects of early or delayed provision of an ankle-foot orthosis in patients with (sub)acute stroke: a randomized controlled trial

Corien DM Nikamp[1,2], Jaap H Buurke[1,3], Job van der Palen[4,5], Hermie J Hermens[1,3] and Johan S Rietman[1,2,6]

Abstract

Objective: To study the six-month clinical effects of providing ankle-foot orthoses at different moments (early or delayed) in (sub)acute stroke; this is a follow-up to a published trial.
Design: Randomized controlled trial.
Setting: Rehabilitation centre.
Subjects: Unilateral hemiparetic stroke subjects maximal six weeks post-stroke with indication for ankle-foot orthosis use.
Interventions: Subjects were randomly assigned to early (at inclusion; week 1) or delayed provision (eight weeks later; week 9).
Outcome measures: Functional tests assessing balance and mobility were performed bi-weekly for 17 weeks and at week 26.
Results: In all, 33 subjects were randomized. No differences at week 26 were found between both groups for any of the outcome measures. However, results suggest that early provision leads to better outcomes in the first 11–13 weeks. Berg Balance Scale ($P = 0.006$), Functional Ambulation Categories ($P = 0.033$) and 6-minute walk test ($P < 0.001$) showed significantly different patterns over time. Clinically relevant but statistically non-significant differences of 4–10 weeks in reaching independent walking with higher balance levels were found, favouring early provision.
Conclusion: No six-month differences in functional outcomes of providing ankle-foot orthoses at different moments in the early rehabilitation after stroke were found. Results suggest that there is a

[1]Roessingh Research and Development, Enschede, The Netherlands
[2]Department of Biomechanical Engineering, MIRA – Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands
[3]Department of Biomedical Signals and Systems, MIRA – Institute for Biomedical Technology and Technical Medicine, University of Twente, Enschede, The Netherlands
[4]Medisch Spectrum Twente, Medical School Twente, Enschede, The Netherlands
[5]Department of Research Methodology, Measurement and Data Analysis, University of Twente, Enschede, The Netherlands
[6]Department of Amputation and Orthopedics, Roessingh Centre for Rehabilitation, Enschede, The Netherlands

Corresponding author:
Corien DM Nikamp, Roessingh Research and Development, Roessinghsbleekweg 33B, PO Box 310, 7500 AH Enschede, The Netherlands.
Email: c.nikamp@rrd.nl

period of 11–13 weeks in which early provision may be beneficial, possibly resulting in early independent and safe walking. However, our study was underpowered. Further research including larger numbers of subjects is warranted.

Keywords
Ankle-foot orthosis, stroke, six-month effect, timing of provision, randomized controlled trial

Received: 21 March 2017; accepted: 14 April 2017

Introduction

Ankle-foot orthoses are often used to minimize gait deviations and to improve walking after stroke. Despite the frequent use of ankle-foot orthoses, clinical relevant questions, such as long-term effects of using an orthosis after recent stroke and when to start treatment, remain unanswered.[1] Most studies investigating the effects of ankle-foot orthosis use after stroke reported the direct or short-term effects and included chronic patients with independent walking ability. Most of them were already using an orthosis in everyday life.[1] Studies including longer follow-up periods of three to six months did not investigate the actual provision of orthosis early after stoke but compared different orthosis designs with each other,[2] or orthosis use was compared with functional electrical stimulation,[3–5] conventional physical therapy[6] or no orthosis.[7] Studies investigating when to start using ankle-foot orthoses are scarce. Wang et al.[8] found that an orthosis improved balance, gait speed and cadence in patients less than six months after stroke, whereas effectiveness was minimal in patients more than 12 months after stroke.[8]

We previously reported the short-term results of an explorative randomized controlled trial to study the effects of providing off-the-shelf ankle-foot orthoses on two different moments post-stroke.[9] We included patients within six weeks post-stroke and provided them with an ankle-foot orthosis in week 1 (early) or 9 (delayed) of the study. The effects of provision were studied after two weeks. We found that the positive effects were more pronounced in the early group compared to the delayed group. This suggests that early provision may be beneficial. This article reports on the six-month outcomes of the randomized controlled trial. Our primary aim was to investigate the six-month clinical effects of providing ankle-foot orthoses at different moments (early or delayed) in the rehabilitation post-stroke. The secondary aim was to study whether different timing affects functional improvement over time and whether reaching levels related to independence and safety of walking differed between the two groups. We hypothesized that early provision is more beneficial.

Methods

We designed a single-centre randomized controlled parallel group study. The study was approved by the Medical Ethical Committee Twente and registered in the 'Nederlands Trial Register', number NTR1930. A detailed description of our study design and patient inclusion can be found in our previous paper.[9] In summary, we recruited unilateral ischaemic or haemorrhagic stroke subjects from the Roessingh Centre for Rehabilitation in Enschede, the Netherlands. Subjects were maximal six weeks post-stroke and had an indication for use of an ankle-foot orthosis. Subjects were randomized to either (1) ankle-foot orthosis provision at inclusion, in study week 1 (early group) or (2) delayed provision after eight weeks, in study week 9 (delayed group). Subjects were provided with one of the three commonly used types of off-the-shelf, non-articulated, posterior leaf design, polyethylene or polypropylene ankle-foot orthoses: flexible, semi-rigid or rigid (Basko Healthcare, Zaandam, the Netherlands) (see Figure 1). The type

Figure 1. Three types of ankle-foot orthoses used in the study.
Types of ankle-foot orthoses, from left to right: (1) polyethylene, non-articulated orthosis with two crossed posterior steels and open heel, most flexible type; (2) semi-rigid, polypropylene, non-articulated orthosis with two crossed posterior steels and open heel, larger posterior steel compared to type 1; (3) rigid, polypropylene, non-articulated orthosis with closed posterior steel and closed heel.

of orthosis was chosen in week 1 (early group) or week 9 (delayed group). A full description of the orthosis selection was published previously.[9]

Baseline measurements were performed without orthosis in week 1 for both groups. Measurements were repeated every other week until week 17, with follow-up measurements in week 26 (see Figure 2). Subjects in the early group were provided with the orthosis after the measurements in week 1, and subjects in the late group did not use an orthosis in this period and were provided with the orthosis eight weeks later, after the measurements in week 9. After provision, all measurements were performed with ankle-foot orthosis.

At inclusion, demographic data were recorded. The primary outcome measure was comfortable walking speed, assessed with the 10-meter walk test.[10] Secondary, balance was assessed using the Berg Balance Scale,[11] independent of walking with the Functional Ambulation Categories,[12] walking ability with the 6-minute walk test[13] and functional mobility with the Timed Up and Go Test[14] and Stairs Test.[15] Selective muscle control and isometric contraction were assessed with the Motricity Index, lower limb part.[16] The Rivermead Mobility Index[17] and Barthel Index[18] were used to assess mobility during activities of daily life. All tests that included walking were only performed in subjects who could walk without physical support (minimum Functional Ambulation Categories level 3 required) at the time of the measurement.

Data analysis

IBM SPSS Statistics version 19 (IBM SPSS Statistics, Chicago, IL, USA) was used for data analysis. The level of significance for all analyses was set at $P<0.05$. Normality was checked using the Shapiro–Wilk test in all analyses. In case walk tests could not be performed because the Functional Ambulation Categories is less than 3, the 10-meter walk test and 6-minute walk test were set at 0.0 m/s and 0 m, respectively, while the Timed Up and Go and Stairs Tests were treated as missing values because using 0 second for these outcome measures would mean an infinitely fast performance of the test.

Baseline data are presented as mean (SD) or median (interquartile ranges (IQR)) and tested as appropriate. Six-month effects were studied by comparing outcome results of the early and delayed group at week 26 using independent samples *t*-tests (normal distribution) or Mann–Whitney *U*-tests (non-normal distribution), as appropriate. Secondary, generalized estimating equation analyses were performed to compare group by time interactions, using data from all functional tests from weeks 1 to 17 (measured every other week) and week 26. Survival analyses (log-rank test) were performed to compare

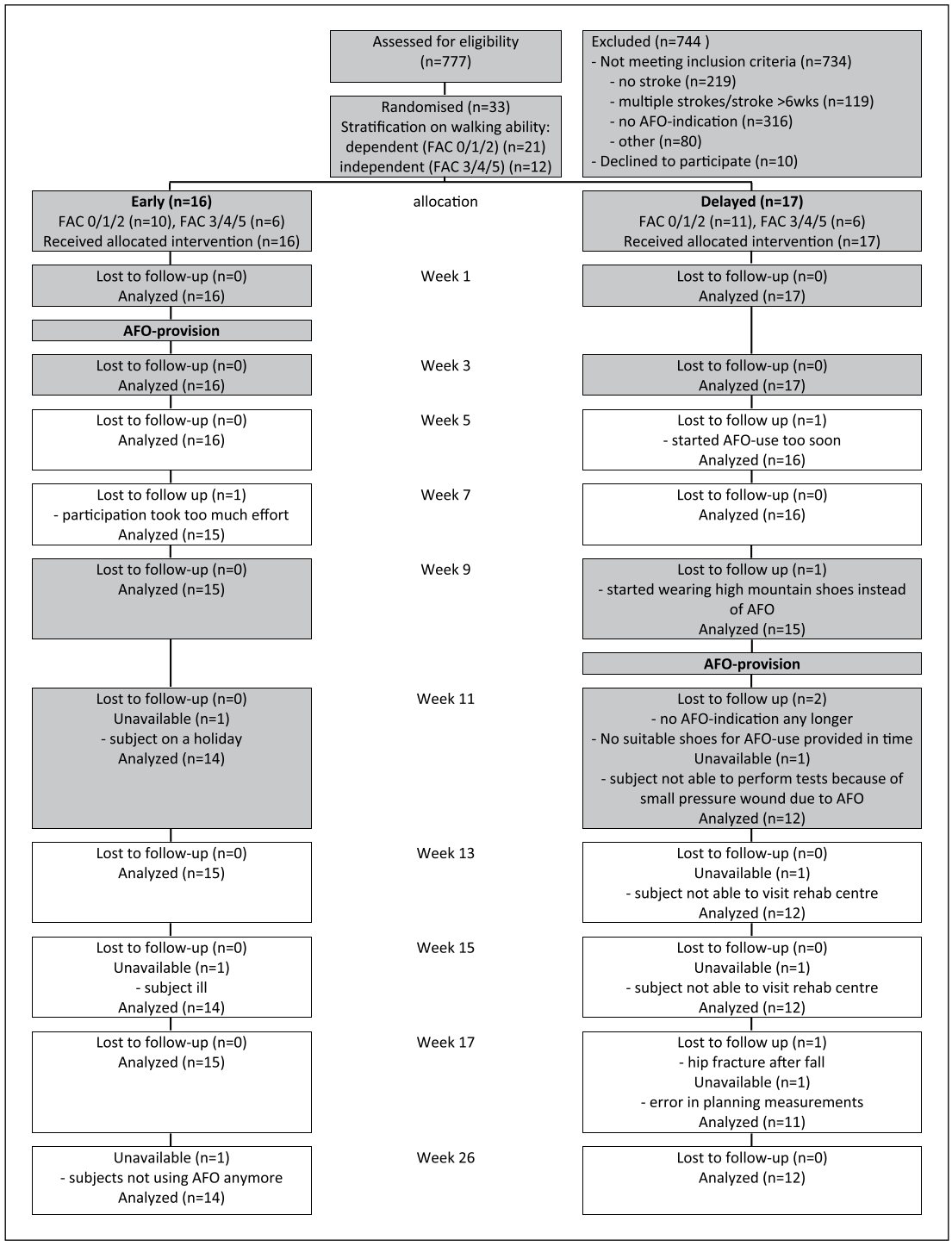

Figure 2. Consort flowchart.
The grey areas indicate previously published data.

Table 1. Subject characteristics at inclusion.

		Total ($N=33$)	Early ($n=16$)	Delayed ($n=17$)
Sex (male/female)[a]		20/13	10/6	10/7
Age (years)[b]		57.2 (9.2)	56.9 (9.6)	57.5 (9.1)
Time since stroke at inclusion (days)[b]		31.4 (6.3)	32.0 (6.2)	30.8 (6.5)
FAC level at inclusion (0/1/2/3/4/5)[c]		0/7/14/11/1/0	0/3/7/6/0/0	0/4/7/5/1/0
Affected body side (left/right)[a]		16/17	8/8	8/9
Type of stroke (ischemic/haemorrhagic)[c]		27/6	14/2	13/4
Type of AFO at provision[d] (flexible/semi-rigid/rigid/no orthosis)[c]		27/0/3/3	14/0/2/0	13/0/1/3
Sensation[e]	Tactile (normal/impaired/absent)[c]	26/4/3	13/1/2	13/3/1
	Propriocepsis (normal/impaired/absent)[c]	26/6/1	13/2/1	13/4/0
Mini-Mental State Examination[f]		27.0 (23.5–28.0)	27.0 (25.3–28.0)	27.0 (22.5–28.0)

FAC: Functional Ambulation Categories; AFO: ankle-foot orthosis.
Mean (SD) or median (interquartile range (IQR)) are presented.
[a]Pearson chi-square test (two-tailed).
[b]Independent samples *t*-test.
[c]Fisher exact test.
[d]Three subjects were not provided with an orthosis: one dropped out before orthosis provision (week 5); one preferred wearing high mountain shoes instead of an orthosis, and one had no indication any longer at the moment of provision in week 9. Furthermore, two subjects (both early) changed from a flexible to a semi-rigid type during the study (in weeks 4 and 8, respectively) since support provided by the flexible type appeared to be insufficient.
[e]Tested with Erasmus MC modifications to the Nottingham Sensory Assessment, lower limb part.
[f]Mann–Whitney *U*-test with median (IQR).

both groups in reaching clinical relevant cut-off points related to independence and safety of walking. One minus survival functions were used for depicting results. The following cut-off points were used: Functional Ambulation Categories $\geqslant 3$, which relates to the ability to walk without physical support of another person; Berg Balance Scale $\geqslant 45$ points, which relates to a decreased fall risk;[19] $\geqslant 0.27$ m/s for walking speed, which relates to the functional walking category 'unlimited household walker' as defined by Perry et al.[20]

Results

In all, 33 subjects were included, 16 in the early group and 17 in the delayed group (see Table 1). There were no significant differences at baseline between both groups. Figure 2 details the participant flow through the study. Six subjects dropped out (one early, five delayed). In addition, data of six of the included subjects were unavailable in one of the measurement weeks due to practical reasons (e.g. holiday, illness; see Figure 2).

At week 26, no significant differences were found between the early and delayed groups for any of the outcome measures (Table 2).

Figure 3 shows the mean (SE) scores of both the early and delayed groups for all outcome measures during the study. In general, both groups improved over time. Furthermore, the early group showed better outcomes on most functional tests in the first 11–13 weeks of the study compared to the delayed group, except for the Motricity Index and the Stairs Test. The Berg Balance Scale ($P=0.006$), Functional Ambulation Categories ($P=0.033$) and 6-minute walk test ($P<0.001$) showed significantly different patterns over time.

Results of the survival analyses are shown in Figure 4. All subjects reached Functional Ambulation Categories $\geqslant 3$ within the follow-up period of the study (early: latest in week 5; delayed: latest in week 15). The cut-off points of $\geqslant 45$ points for Berg Balance Scale and $\geqslant 0.27$ m/s for walking speed were reached by all subjects in the early group (both by week 11), while three subjects in the delayed group did not reach these levels. None

Table 2. Results at week 26.

	N	Early	*N*	Delayed	Independent samples *t*-test Early group–Delayed group (95% CI)	*P*
10MWT (m/s)	14	0.72 (0.37–0.93)	12	0.82 (0.26–0.87)		0.700[a]
BBS	14	52.5 (48.8–55.3)	12	53.0 (44.5–53.8)		0.534[a]
FAC	14	5.0 (4.0–5.0)	12	4.5 (3.3–5.0)		0.256[a]
6MWT (m)[b]	14	234 (126)	11	244 (134)	−10.2 (−118 to 98)	0.846
ST[c]	13	50.6 (23.9)	8	49.8 (19.5)	0.8 (−20.3 to 21.8)	0.942
TUG (seconds)	14	16.9 (11.8–27.8)	12	14.3 (12.3–40.8)		0.837[a]
RMI	14	13.0 (12.0–14.0)	12	13.5 (9.3–14.0)		1.000[a]
BI	14	19.5 (18.5–20.0)	12	19.5 (14.8–20.0)		0.562[a]
MI	14	49.8 (17.9)	12	56.8 (24.7)	−7.0 (−24.3 to 10.3)	0.414

10MWT: 10-meter walk test; BBS: Berg Balance Scale; FAC: Functional Ambulation Categories; 6MWT: 6-minute walk test; ST: Stairs Test; TUG: Timed Up and Go; RMI: Rivermead Mobility Index; BI: Barthel Index; MI: Motricity Index.
Mean (SD) or median (interquartile range) are presented.
[a]Mann–Whitney *U*-test.
[b]Data of one subject (delayed) are missing; subject was too tired to perform the test.
[c]Data of one (early) and four (delayed) subjects are missing; subjects were not able to walk the stairs.

of the outcomes reached statistical significance (Functional Ambulation Categories $P=0.101$; Berg Balance Scale $P=0.102$; walking speed $P=0.183$).

Discussion

This study showed no differences in functional outcomes after 26 weeks of early compared to delayed provision of an ankle-foot orthosis after recent stroke. However, we must emphasize that our study has included only a limited number of patients and is therefore underpowered. Despite the small number of patients, we were able to find trends with respect to the pattern of functional improvement over time and with respect to reaching levels of independence and safety of walking. We found that the early group had higher scores in the beginning of the study (during the first 11–13 weeks) for most outcome measures compared to the delayed group. In addition, the early group could walk up to 10 weeks earlier without physical support of another subject compared to the delayed group. Balance levels related to less fall risk and walking speed related to household walking were reached four to six weeks earlier, respectively. The differences were non-significant, but these trends suggest that there may be a period of time in which early provision may be beneficial. This is valuable information for clinicians because early orthosis provision may therefore increase the ability to perform task-specific rehabilitation exercises with high repetitions and in a meaningful context – conditions known to be important for better outcomes.[21] Furthermore, this may also reduce the length of in-clinic stay. Therefore, a new study with larger number of patients is warranted.

An important strength of this study is that we took the timing of providing ankle-foot orthoses into account. We included subjects early after stroke, also in case they had no independent walking ability. This strengthens the transfer of our results to daily clinical practice. We found indications that there is a period of time in which early provision is beneficial. These results match with observations by Stinear et al.[22] who stated that 'the benefits of treatments delivered in the early stage could go undetected if the primary outcome is $\geqslant$3 months after stroke, by which time the control group may have caught up'.

The main limitation of our study is the small sample size as discussed. Furthermore, six subjects dropped out from the study (one early, five delayed) for various reasons. We have no reasons to believe that drop-out was related to the intervention. The contrast of our intervention could have been larger in case we included a control group that was not

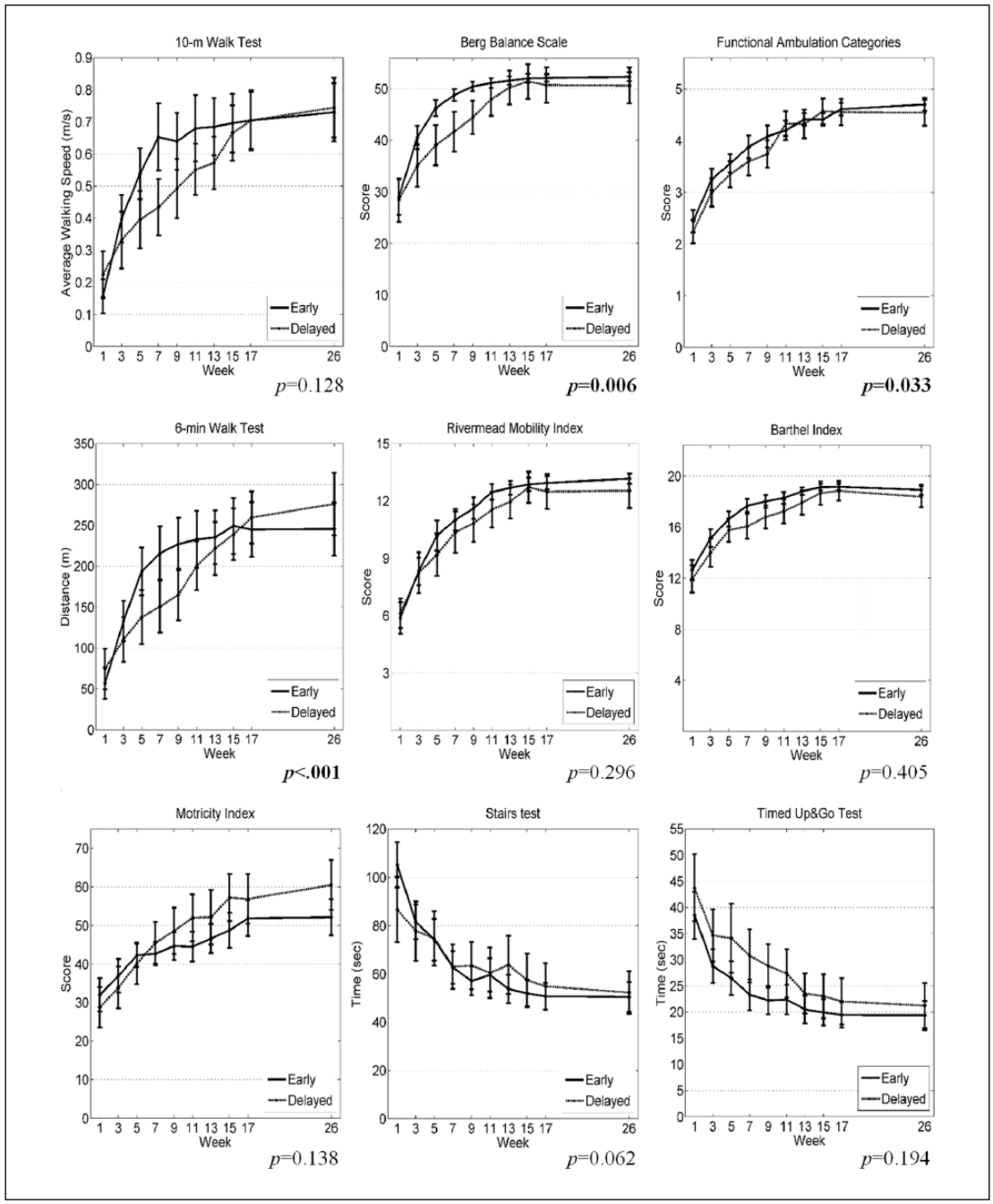

Figure 3. Generalized estimating equation analysis to compare the early and delayed groups over time.
Generalized estimating equation analysis for all functional tests is shown to compare group by time interactions. Early (solid line) and delayed (dashed line) groups are depicted. Mean (SE) are shown during all measurement weeks. Note that the early group was provided with an AFO after the measurements in week 1 and the delayed group after the measurements in week 9. Increasing scores represent better performance on a particular test, except for the Stairs Test and the Timed Up and Go Test, where decreasing scores represent better (faster) performance of the test.

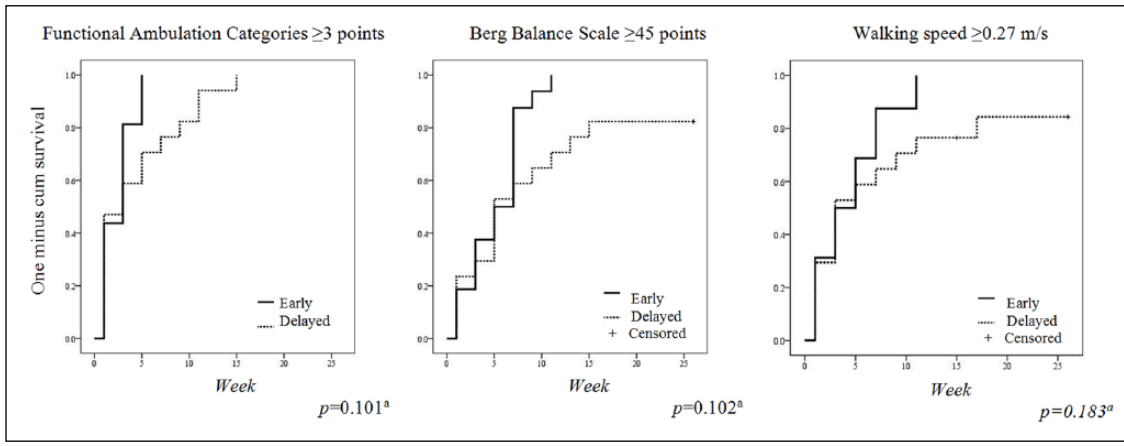

Figure 4. Survival analysis reaching clinical relevant cut-off points.
The vertical axis represents the proportion of subjects that reached the cut-off point – Functional Ambulation Categories: ⩾3 points; Berg Balance Scale: ⩾45 points; and walking speed during 10-meter walk test: ⩾0.27 m/s. The horizontal axis represents the measurement weeks of the study. Solid line: early group; dashed line: delayed group. [a]Log-rank test. For Berg Balance Scale and walking speed, data of three subjects (all delayed) are censored (marked with +) as they did not reach the cut-off point within the measurement period. The last subject in the delayed group who did reach the cut-off point for Berg Balance Scale and walking speed reached this in weeks 15 and 17, respectively.

provided with an AFO, instead of a delayed provision. This would increase the prospects of detecting differences. Within the generalized estimating equation analysis, missing data are assumed to be 'missing at random'. However, this was not the case for missing data of the Timed Up and Go Test and the Stairs Test (Functional Ambulation Categories <3 or not able to negotiate stairs). Since no other options were available, we chose to perform the generalized estimating equation analysis, including the non-random missing data, so these results should be interpreted with caution.

Clinical messages

- Early provision of an ankle-foot orthosis after stroke was associated with a better functional outcome at about 12 weeks, but at 26 weeks there were no detectable differences. The study was not powered to detect differences at six months.
- Patients with early provision of ankle-foot orthoses showed a general trend towards earlier independence in mobility, warranting further and larger trials.

Acknowledgements

The authors thank the patients and staff from the Roessingh Centre for rehabilitation, Enschede, the Netherlands, and staff from Roessingh Rehabilitation Technology, Enschede, the Netherlands for their participation and cooperation to the study. Furthermore, they also thank Basko Healthcare for providing the ankle-foot orthoses.

Author contributors

C.D.M.N. helped with the conception and design, measurements, analysis, interpretation of data, and drafting and final approval of the article. J.H.B, H.H. and J.S.R. helped with conception and design, interpretation of data, revising and final approval of the article. J.v.d.P helped with the conduction of the analysis, interpretation of data, revising and final approval of the article.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship and/or publication of this article: The ankle-foot orthoses used in this study were provided by Basko Healthcare, Zaandam, the Netherlands. Basko was not involved in designing, collecting data or the statistical analysis of study. In addition, they had no role in writing the article and the decision to submit the article for publication.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship and/or publication of this article: This work was supported by grants from the 'Dutch Ministry of Health, Welfare and Sport' and 'Stichting Hulpfonds Het Roessingh'.

References

1. Tyson SF and Kent RM. Effects of an ankle-foot orthosis on balance and walking after stroke: a systematic review and pooled meta-analysis. *Arch Phys Med Rehabil* 2013; 94: 1377–1385.
2. de Sèze M, Bonhomme C, Daviet J, et al. Effect of early compensation of distal motor deficiency by the Chignon ankle-foot orthosis on gait in hemiplegic patients: a randomized pilot study. *Clin Rehabil* 2011; 25(11): 989–998.
3. Everaert DG, Stein RB, Abrams GM, et al. Effect of a foot-drop stimulator and ankle-foot orthosis on walking performance after stroke: a multicenter randomized controlled trial. *Neurorehabil Neural Repair* 2013; 27(7): 579–591.
4. Kluding PM, Dunning K, O'Dell MW, et al. Foot drop stimulation versus ankle foot orthosis after stroke: 30-week outcomes. *Stroke* 2013; 44(6): 1660–1669.
5. Bethoux F, Rogers HL, Nolan KJ, et al. Long-term follow-up to a randomized controlled trial comparing peroneal nerve functional electrical stimulation to an ankle foot orthosis for patients with chronic stroke. *Neurorehabil Neural Repair* 2015; 29(10): 911–922.
6. Pomeroy VM, Rowe P, Clark A, et al. A randomized controlled evaluation of the efficacy of an ankle-foot cast on walking recovery early after stroke: SWIFT cast trial. *Neurorehabil Neural Repair* 2016; 30(1): 40–48.
7. Erel S, Uygur F, Simsek IE, et al. The effects of dynamic ankle-foot orthoses in chronic stroke patients at three-month follow-up: a randomized controlled trial. *Clin Rehabil* 2011; 25: 515–523.
8. Wang RY, Yen L, Lee CC, et al. Effects of an ankle-foot orthosis on balance performance in patients with hemiparesis of different durations. *Clin Rehabil* 2005; 2005: 19(1): 37–44.
9. Nikamp CD, Buurke JH, Van der Palen J, et al. Early or delayed provision of an ankle-foot orthosis in patients with acute and subacute stroke: a randomized controlled trial. *Clin Rehabil* 2017; 31(6): 798–808.
10. Wade DT (ed.). *Measurements in neurological rehabilitation*. Oxford: Oxford University Press, 1992.
11. Berg K, Wood-Dauphinee S, Williams JI, et al. Measuring balance in the elderly: preliminary development of an instrument. *Physiother Can* 1989; 1989(41): 304–311.
12. Holden MK, Gill KM, Magliozzi MR, et al. Clinical gait assessment in the neurologically impaired. Reliability and meaningfulness. *Phys Ther* 1984; 64(1): 35–40.
13. Eng JJ, Chu KS, Dawson AS, et al. Functional walk tests in individuals with stroke: relation to perceived exertion and myocardial exertion. *Stroke* 2002; 33(3): 756–761.
14. Podsiadlo D and Richardson S. The timed 'Up & Go': a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc*. 1991; 39(2): 142–148.
15. De Wit D, Buurke J, Nijlant J, et al. The effect of an ankle-foot orthosis on walking ability in chronic stroke patients: a randomized controlled trial. *Clin Rehabil* 2004; 18: 550–557.
16. Collin C and Wade D. Assessing motor impairment after stroke: a pilot reliability study. *J Neurol Neurosurg Psychiatry* 1990; 1990: 53(7): 576–579.
17. Collen FM, Wade DT, Robb GF, et al. The Rivermead Mobility Index: a further development of the Rivermead Motor Assessment. *Int Disabil Stud* 1991; 13(2): 50–54.
18. Collin C, Wade DT, Davies S, et al. The Barthel ADL Index: a reliability study. *Int Disabil Stud* 1988; 10(2): 61–63.
19. Piotrowski A and Cole J. Clinical measures of balance and functional assessment in elderly persons. *Aust J Physiother* 1994; 40(3): 183–188.
20. Perry J, Garrett M, Gronley JK, et al. Classification of walking handicap in the stroke population. *Stroke* 1995; 26(6): 982–989.
21. Veerbeek JM, Van Wegen E, Van Peppen R, et al. What is the evidence for physical therapy poststroke? A systematic review and meta-analysis. *PLoS ONE* 2014; 9(2): e87987.
22. Stinear C, Ackerley S and Byblow W. Rehabilitation is initiated early after stroke, but most motor rehabilitation trials are not: a systematic review. *Stroke* 2013; 44(7): 2039–2045.